REMARKS

The claims have been amended to obviate the rejection under 35 U.S.C. § 112, paragraph 1. Support for new claim 17 is found on page 8 at lines 20-24. Support for claim 18 is found in the examples. Support for claims 19 and 20 is found in claims 7 and 8 previously pending. The remaining claims depend from claims 17-20. New claims 21-22 are simply reworded forms of former claims 1 and 6. These correspond directly to the elected invention. No new matter is added and entry of the amendment is respectfully requested.

Applicants believe the amendment is in accordance with their election as the Office recognizes the subject matter of claims 17-20 as an acceptable alternative to the subject matter of former claims 1-13. New claims 21-22 are clearly substitute forms of claims 1 and 6 previously pending, but slightly rephrased. The Office has examined the subject matter of all of these claims and thus no undue burden is believed imposed on the Office by these amendments.

The outstanding rejections are addressed as follows:

Claims 1-13 were rejected for asserted lack of enablement. The Office kindly acknowledges that the specification is enabling for a method of decreasing the allergenicity of 2S albumin ber E1 from Brazil nuts by alkylating and reducing the protein. The scope of claim 1 is substantially that acknowledged as enabled by the Office except that the 2S albumin is not limited to the 2S albumin from Brazil nuts.

Applicants believe that this scope is justified in view of the knowledge in the art concerning 2S albumins. Enclosed herewith is a copy of chapter 2 of a monograph "Detecting Allergens in Food" published by CRC Press. The subject of chapter 2 is "Classifying Food Allergens." The 7th page of this chapter discusses the 2S albumins as a family in the second full paragraph. This

paragraph states that this family is of "structurally related homologous proteins" and that these proteins are "rich in alpha helices and are held together by four disulfide bonds involving eight conserved cysteine residues." The "typical" 2S albumins include the Brazil nut 2S albumin.

Thus, it would appear that the family is sufficiently structurally analogous that it is reasonable to extrapolate from the results presented in the application for a Brazil nut 2S albumin to 2S albumins in general.

The Office correctly notes that reduction in alkylation alters the conformational structure of food allergens, and it is believed that in view of the similarity of the 2S albumins to each other, similar alterations would occur and that therefore it would indeed be predictable that reducing the disulfide linkages and alkylating the resultants would provide similar results in the remaining 2S proteins.

Thus, new claims 17-20 should be considered free, now, of this rejection. As to claims 21-22, applicants are enclosing an article by Nowak-Wegrzyn, A., *Pediatrics* (2003) 111:1672-1680 describing means to desensitize subjects to allergens. As noted in the paragraph bridging pages 1675 — 1676, allergic diseases are characterized by the relative predominance of Th2 type responses (i.e. mediated by IgE) over Th1 responses (i.e. mediated by IgG1), and most of the immunomodulatory therapeutic approaches to food allergy operate on the premise of restoring the Th1/Th2 balance (or activating regulatory T-lymphocytes). As described in the specification on page 3, beginning at line 25, it is possible to effectively desensitize the individual to the allergen because the modified allergen leads to a reduction or prevention of the production of specific IgE antibodies, but IgG1 antibodies are still made thus skewing the immune response from a Th2 mediated reaction toward a Th1 mediated reaction, thus desensitizing the individual. As shown in

the specification in the example on pages 13-22, Figure 3 described on page 19 shows that the reduced and alkylated form of the Brazil nut 2S albumin failed to elicit IgE responses, while as shown in Figure 2, the reduced and alkylated 2S albumin was still able to generate IgG1 response (although not as strong). As explained on page 22, the IgG1 response is a Th1 response while the IgG2a and IgE responses are Th2 responses.

The enclosed article by Nowak-Wegrzyn, on page 1677 also describes, in the paragraph bridging the right and left-hand columns, that engineered allergens that result in reduced IgE, but retain IgG responses decreased symptoms on oral peanut challenge compared with a control group treated with the native allergen. Page 1678 further verifies under "peptide immunotherapy" that eliminating IgE bonding is associated with said therapy.

Thus, it was known in the art at the time the application was filed that tipping the balance between IgE responses and IgG1 responses results in desensitization. On this basis, applicants believe claims 21-22 are enabled.

It is believed that the remainder of this rejection is moot in view of the cancellation of claims 9-11.

Claims 1-13 were also rejected as assertedly lacking written description on the grounds of lack of possession. This appears not to reside in any failure of the application itself to describe the claimed subject matter (which it clearly does on page 3-4 and in the example), but rather appears to be a modified form of the rejection for lack of enablement. Applicants arguments with respect to enablement apply here as well. Indeed, because of the similarity among 2S albumins, the specification does "clearly allow persons of ordinary skill in the art to recognize (that the inventor) invented what is (now) claimed."

In view of the amendment to the claims and the foregoing discussion, both rejections based on 35 U.S.C. § 112, paragraph 1, may be withdrawn.

Claims 1-13 were rejected as assertedly anticipated by WO02/074250 (Panacea). The Examiner is correct that Panacea teaches a method of modifying a protein food allergen by reduction and alkylation. The Office asserts that one of these allergens subject to this procedure would be a 2S albumin, citing Appendix 8. Respectfully, this falls far short of anticipation.

It is established that not only must all of the elements of a claimed subject matter be disclosed in an anticipating document, they must be disclosed in the arrangement required by the instant claims (*Net MoneyIn, Inc. v. VeriSign, Inc.,* 545 F3d 1359, 1369, 88 USPQ2d 1751 (Fed. Cir. 2008). That is not the case here. The generic discussion of reduction and alkylation of food allergens in Panacea is never applied specifically to a 2S albumin. Further, to consider the cited document to be anticipatory would be directly contrary to the position taken by the Office with regard to the present application — namely that it is unpredictable whether reduction and alkylation that is successful in one protein will also be successful in another. It cannot be true that all of the proteins in Appendix 8 can successfully be rendered less all allergenic by this method, and surely in light of the discussion in regard to the present application, the Examiner must agree with this. Merely including the Brazil nut 2S albumin on a laundry list of food allergens is insufficient to constitute anticipation. As held in *Continental Can Co. USA, Inc. v. Monsanto Co.*, 948 F2d 1264, 20 USPQ2d 1746 (Fed. Cir. 1991), in order to anticipate, the claimed subject matter must be a direct and inevitable result of the cited disclosure. It cannot be a matter of probabilities. There is no inevitable result here.

Among the exemplified peanut antigens is this document is Ara h 2 which is the 2S albumin in peanuts. (See Table 2.1 of the enclosure.) This example does not, of course, anticipate since it does not employ reduction and alkylation. This example does not render the invention obvious either since, although Panacea is clearly aware that reduction and alkylation are methods to diminish allergenicity, for this particular protein, only production of mutants is described. (See page 100-126 of Panacea.) In particular, starting on page 113, the IgE binding epitopes are mapped and the critical amino acids are set forth in Table 25 on page 117; T cell epitopes are also mapped. Table 26 sets forth the list of mutants and does not even include cysteine-depleted mutants. Thus, the reader of the enclosed document would conclude that the authors found it necessary to go through the complicated process of preparing mutants rather than undertaking the relatively simple processes of reduction and alkylation. In effect, Panacea teaches away from the invention as now claimed.

In view of the foregoing, the outstanding rejection over Panacea may be withdrawn.

Conclusion

Claims 17-20 have been limited almost to the scope acknowledged as enabled and described by the Office; the only enlargement of scope is to include what are known in the art as very similar homologous proteins. The nexus between the results shown in the specification for reduced and alkylated Brazil nut 2S albumin with respect to IgG and IgE are shown as known in the art to correlate to desensitization to the allergen. Thus, claims 21-22 are enabled and described as well. The cited Panacea document fails to anticipate the invention as it does not specifically tie 2S albumin to treatment by redundant and alkylation. Instead, it teaches away by illustrating reducing

allergenicity of the Ara h 2 protein by mutation. Accordingly, applicants believe that claims 17-22 are in a position for allowance and passage of these claims to issue is respectfully requested.

Should minor issues remain that could be resolved over the phone, a telephone call to the undersigned is respectfully requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 677132000200.

Respectfully submitted,

Dated: May 28, 2010

By: / Kate H. Murashige /

Kate H. Murashige
Registration No.: 29,959
MORRISON & FOERSTER LLP
12531 High Bluff Drive, Suite 100
San Diego, California 92130-2040
Telephone: (858) 720-5112
Facsimile: (858) 720-5125